CLAIMS

[Claim 1]

A composite comprising a neural retina, a retinal pigment epithelial cell sheet, and a hydrogel, wherein

the neural retina and the retinal pigment epithelial cell sheet are derived from a human pluripotent stem cell respectively;

in the neural retina, a neural retinal layer including at least a photoreceptor layer is formed, wherein the photoreceptor layer comprises at least one or more cells selected from the group consisting of a photoreceptor cell, a photoreceptor precursor cell and a retinal precursor cell;

a melting point of the hydrogel is from 20°C to 40°C; and

the whole of the neural retina and the retinal pigment epithelial cell sheet is embedded in the hydrogel, tangent directions of the respective surfaces of the neural retina and the retinal pigment epithelial cell sheet are approximately parallel, an apical surface of the neural retina and an apical surface of the retinal pigment epithelial cell sheet face each other, and the neural retina and the retinal pigment epithelial cell sheet are separated by the hydrogel from each other without contact.

[Claim 2]

The composite according to claim 1, wherein a jelly strength of the hydrogel is from 1000 g to 2000 g.

[Claim 3]

The composite according to claim 1 or 2, wherein a concentration of the hydrogel is from 10% to 50% by weight.

[Claim 4]

The composite according to any one of claims 1 to 3, wherein a pH of the hydrogel is from 6.5 to 7.5.

[Claim 5]

The composite according to any one of claims 1 to 4, wherein the hydrogel has biodegradability.

[Claim 6]

The composite according to any one of claims 1 to 5, wherein the hydrogel is a hydrogel of gelatin.

[Claim 7]

The composite according to claim 6, wherein the gelatin is alkali-treated and/or heat-treated gelatin.

[Claim 8]

The composite according to any one of claims 1 to 7, wherein

the neural retina is a neural retina obtained from a cell aggregate obtained by differentiating a human pluripotent stem cell,

the cell aggregate comprises at least a first epithelial tissue and a second epithelial tissue, wherein the first epithelial tissue contains a human neural retina, and the second epithelial tissue has continuity of a slope of a tangent line to a surface different from continuity of a slope of a tangent line to the surface of the first epithelial tissue, and contains a cell other than a retinal cell and/or a retinal pigment epithelial cell, and

the neural retina contains a region on the first epithelial tissue most distant from the second epithelial tissue in the cell aggregate.

[Claim 9]

A method for producing a composite comprising a neural retina, a retinal pigment epithelial cell sheet, and a hydrogel, wherein

the neural retina and the retinal pigment epithelial cell sheet are derived from a human pluripotent stem cell respectively;

in the neural retina, a neural retinal layer including at least a photoreceptor layer is formed, wherein the photoreceptor layer comprises at least one or more cells selected from the group consisting of a photoreceptor cell, a photoreceptor precursor cell and a retinal precursor cell; and

a melting point of the hydrogel is from 20°C to 40°C,

the method comprising:

(1) a first step of loading either one of the retinal pigment epithelial cell sheet and the neural retina in a container;

(2) a second step of adding a hydrogel in a fluid state to the container loaded with the either one of the retinal pigment epithelial cell sheet and the neural retina;

(3) a third step of solidifying the hydrogel by cooling so as to embed the whole of the either one of the retinal pigment epithelial cell sheet and the neural retina to form a first hydrogel layer having the either one of the retinal pigment epithelial cell sheet and the neural retina and the hydrogel;

(4) a fourth step of further loading the other of the retinal pigment epithelial cell sheet and the neural retina on the first hydrogel layer such that tangent directions of the respective surfaces of the either one of the retinal pigment epithelial cell sheet and the neural retina in the first hydrogel layer and the other of the retinal pigment epithelial cell sheet

and the neural retina are approximately parallel and an apical surface of the neural retina and an apical surface of the retinal pigment epithelial cells face each other;

(5) a fifth step of adding a hydrogel in a fluid state to the container further loaded with the other of the retinal pigment epithelial cell sheet and the neural retina; and

(6) a sixth step of solidifying the hydrogel by cooling so as to embed the whole of the first hydrogel layer and the other of the retinal pigment epithelial cell sheet and the neural retina to form a second hydrogel layer having the first hydrogel layer, the other of the retinal pigment epithelial cell sheet and the neural retina, and the hydrogel.

[Claim 10]

The production method according to claim 9, wherein in the third step, cooling to 2°C to 8°C is performed.

[Claim 11]

The production method according to claim 9 or 10, wherein in the sixth step, cooling to 2°C to 8°C is performed.

[Claim 12]

The production method according to any one of claims 9 to 11, further comprising, after the sixth step, (7) a seventh step of preserving the composite at from 10°C to 20°C.

[Claim 13]

The production method according to any one of claims 9 to 12, wherein the jelly strength of the hydrogel is from 1000 g to 2000 g.

[Claim 14]

The production method according to any one of claims 9 to 13, wherein a concentration of the hydrogel is from 10% to 50% by weight.

[Claim 15]

The production method according to any one of claims 9 to 14, wherein a pH of the hydrogel is from 6.5 to 7.5.

[Claim 16]

The production method according to any one of claims 9 to 15, wherein the hydrogel has biodegradability.

[Claim 17]

The production method according to any one of claims 9 to 16, wherein the hydrogel is a hydrogel of gelatin.

[Claim 18]

The production method according to claim 17, wherein the gelatin is alkali-treated and/or heat-treated gelatin.

[Claim 19]

The production method according to any one of claims 9 to 18, wherein

the neural retina is a neural retina obtained from a cell aggregate obtained by differentiating a human pluripotent stem cell,

the cell aggregate comprises at least a first epithelial tissue and a second epithelial tissue, wherein the first epithelial tissue contains a human neural retina, and the second epithelial tissue has continuity of a slope of a tangent line to a surface different from continuity of a slope of a tangent line to the surface of the first epithelial tissue, and contains a cell other than a retinal cell and/or a retinal pigment epithelial cell, and

the neural retina contains a region on the first epithelial tissue most distant from the second epithelial tissue in the cell aggregate.

[Claim 20]

A pharmaceutical composition comprising the composite according to any one of claims 1 to 8 as an active ingredient.

[Claim 21]

A therapeutic medication for a disease caused by a disorder of a retinal tissue or a damage of a retinal tissue, comprising the composite according to any one of claims 1 to 8.

[Claim 22]

A composition for transplantation comprising the composite according to any one of claims 1 to 8.

[Claim 23]

The composition for transplantation according to claim 22, wherein the composition for transplantation is to be transplanted to the eye fundus or into the subretinal space in a patient.

[Claim 24]

~~The~~Use of the composition for transplantation according to claim 23 in the manufacture of a medicament for the treatment of a disease caused by a disorder of a retinal tissue or a damage of a retinal tissue, wherein the composition for transplantation is to be transplanted such that the composite is engrafted in a recipient patient in a condition in which the neural retina of the transplanted composite faces the neural retinal layer of the patient while the retinal pigment epithelial cell sheet of the transplanted composite faces the retinal pigment epithelial layer of the patient.

[Claim 25]

The composite according to any one of claims 1 to 8 for use in the treatment of a disease caused by a disorder of a retinal tissue or a damage of a retinal tissue.

[Claim 26]

Use of the composite according to any one of claims 1 to 8 in the manufacture of a medicament for the treatment of a disease caused by a disorder of a retinal tissue or a damage of a retinal tissue.